

REMARKS/ARGUMENTS

In this Amendment, claims 55-58, 61-65, 68-79, 82, 85, 89-94 and 97 are currently amended and claims 1-54, 66, 67 and 86-88 are canceled without prejudice or disclaimer. Claims 59, 60, 80, 81, 83, 84, 95, 96, 98 and 99 are withdrawn. No new matter has been introduced into the application by virtue of the amended and new claims. A number of the currently amended claims contain formalistic changes to the claim language.

Support for the amended and new claims is found throughout the specification of the instant application and in the prior claims. Specifically, amended claim 55 is supported by the instant specification, *inter alia*, on page 4, lines 1-2 and lines 9-10; and on page 9, lines 1-13.

Accordingly, claims 55-58, 61-65, 68-79, 82, 85, 89-94 and 97 are currently pending in the application.

Applicants respectfully submit that the rejections in the 08/10/2004 Office Action have been addressed herein as if they had been asserted against the presently amended and new claims.

The claims fulfill the requirements of 35 U.S.C. § 112, second paragraph

Claims 55-58, 61-79, 82, 85, 94 and 97 were rejected under 35 U.S.C. §112, second paragraph as allegedly being indefinite. The Examiner has alleged that a double inclusion of elements in a) and c) of claim 55 rendered this claim indefinite with respect to the particular amounts of a) and c).

Applicants submit that presently amended claim 55 moots this rejection. The instant specification discloses that element c) can be in an amount of 0%, thereby reflecting that can be an optional component. *See, e.g.*, the instant specification at page 9, lines 11-12 and 18-19, disclosing that range of plasticizing oil as 0-30% by weight.

In addition, the Examiner mentions the maximum amounts of elements a), b) and c) recited in the composition of claim 55. Applicants submit that presently amended claim 55 moots this aspect of the rejection. Accordingly, it is respectfully submitted that the §112, second paragraph rejection be withdrawn.

The claims fulfill the requirements of 35 U.S.C. § 103(a)

Claims 55-558, 61-79, 82, 85-94 and 97 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable in view of Yamada et al. (U.S. Patent No. 5,362,497), (hereinafter "Yamada"), in view of Wang (U.S. Patent No. 4,299,828), (hereinafter "Wang") and Cooper (U.S. Patent No. 4,552,872), (hereinafter "Cooper").

The Examiner characterizes Yamada as teaching a transdermal composition comprising a pharmaceutically acceptable ingredient, a water soluble absorption enhancer, a fat soluble absorption enhancer and a lower alcohol. Applicants respectfully disagree with this limited characterization of the teachings of Yamada.

It is well established that a reference must be considered for all that it teaches, i.e., as a whole and in its entirety. This includes a consideration of portions that would lead away from the claimed invention. *W L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed.Cir. 1983), as cited in the MPEP §2141.02. Specific sentences should not be taken out of context from prior art references; all of the teachings of the reference must be considered to determine what the reference really teaches. *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve, Inc.* 796 F.2d 443, 230 USPQ 416 (Fed. Cir. 1986). In addition, combining the elements of separate references which do not themselves suggest the combination necessary to obtain a claimed invention is improper. *ACS Hospital Systems, Inc. v. Montifiore Hospital*, 221 USPQ 929, 993 (Fed. Cir. 1984).

Applicants respectfully submit that to be considered for all that it teaches, Yamada must be recognized as also teaching and requiring the inclusion of a super water-absorbent resin as a necessary component of the described transdermal composition. Yamada's contemplated invention relates to the design and preparation of a transdermal therapeutic composition in which the super water-absorbent resin, (e.g., polymers, such as saponified vinyl

acetate-acrylic acid ester copolymers, polyacrylates, anhydride copolymers, etc., as set forth at Col. 3, lines 31-38 of Yamada) must be included to prevent the separation of the fat-soluble components from the water-soluble components. (*See*, Yamada at Col. 2, lines 21-34). Nowhere does Yamada teach omitting the super water-absorbent resin from its composition. If it did, Yamada's composition would not be functional for its intended purpose of effectively delivering the therapeutic.

Yamada solved the problem of separation of ingredients of its described compositions by adding the super water-absorbent resin, which is capable of absorbing water of several tens to more than one thousand times its own weight, thus forming a hydrogel by swelling with water and not releasing the water. (*See*, Yamada at Col. 3, lines 26-30).

Indeed, Yamada owes the action and effects of its described transdermal therapeutic composition to the incorporation of the super water-absorbent resin to prevent the separation of ingredients from one another. (*See, e.g.*, Yamada at Col. 7, lines 3-6). Therefore, it is clearly understood by one having skill in the art that such resin is not an optional ingredient that can be omitted or ignored in Yamada's composition. Rather, the super water-absorbent resin is particularly incorporated into Yamada's composition for a functional purpose, thus making Yamada's compositions distinct from Applicants' presently claimed homogeneous composition.

Yamada generally teaches that a water-soluble absorption enhancer can be combined with a fat soluble enhancer in Yamada's composition that must also contain a super water-absorbent resin to allow Yamada's composition to suit its intended purpose as a transdermal therapeutic and to suppress separation of the component ingredients. (*See*, Yamada at Col. 2, lines 26-30). Thus, Yamada actually teaches to the art that a composition containing only a water-soluble absorption enhancer with a fat soluble enhancer would not function as a useable dermatological composition due to the component ingredients separating from each other in the absence of the resin. Yamada is therefore distinct from Applicants' presently claimed invention, which contains specified amounts of solvent components and viscosity enhancing agent. It is submitted that Yamada teaches away from Applicants' invention considered in its entirety.

Applicants' composition as presently claimed is patentably distinct from that described by Yamada. Applicants have invented homogeneous compositions in which the components do not separate or sediment, but are compatible by virtue of the solvent mixtures as claimed. Indeed, Applicants have solved the problem of incompatibility of ingredients in a biologically active composition and have achieved a homogeneous composition by using the component solvents and mixtures as claimed. In accordance with Applicants' invention, the homogeneous carrier system in which the biologically active agent is dissolved includes a specific combination of solvents for the active agent and a viscosity enhancing agent as a stiffening agent, which imparts a soft and erodible consistency to the composition. (*See*, the instant specification on page 4, lines 30-36).

Applicants' homogeneous carrier system comprises, in admixture, miscible solvent and viscosity enhancing substances in amounts that yield compositions which contain active biological activities. Applicants' homogeneous system solves the problem of separation and non-miscibility of the component ingredients. (*See, e.g.*, Example 1, pages 12-13 of the instant specification). In addition, in Applicants' composition as presently claimed, alkylene glycol is present in a specified amount to provide for mutual dissolution of the unsaturated fatty acid alcohol and the biologically active agent components of Applicants' claimed composition.

Turning to Wang, Wang discloses a composition in the form of a lipophilic stick. In contrast to Applicants' presently claimed composition, the composition of Wang comprises corticosteroids and propylene glycol or 1,3 di-butylene glycol in amounts of 3-10% (*See*, Col. 3, lines 17-22 of Wang). However, the instant invention specifies that the alkylene glycol component be present in an amount of at least 12%. The composition according to the present invention comprises alkylene glycols in an amount that gives a mutual dissolution of the unsaturated fatty acid and the active agent. Unlike Applicants' claimed composition, the composition disclosed in Wang is not a homogeneous composition -- instead it contains dispersed particles.

Given the teaching and suggestion provided by Wang, considered as a whole, if one having skill in the art were to combine Wang with Yamada, the resulting composition would be expected to contain a super water-absorbent resin and propylene glycol or 1,3 di-butylene

glycol in amounts of 3-10%. This is unlike Applicants' invention, which specifies higher amounts of alkylene glycol, and does not lead one to make Applicants' invention as presently claimed. Thus, Yamada and Wang, in combination, do not provide any motivation for the skilled practitioner to make the modifications that are necessary to arrive at Applicants' presently claimed compositions with a reasonable expectation of success. Moreover, there is no teaching or suggestion in Yamada and Wang to combine the teachings of these references so as to achieve Applicants' inventive composition.

Further, if one were to combine the teachings of Yamada, or Yamada and Wang, with Cooper, it is submitted that there is no teaching or suggestion in Cooper that would motivate one having skill in the art to remove the super-absorbent resin from the composition of Yamada, or to formulate the composition of Yamada in the absence of such a resin, to achieve with a reasonable expectation of success a composition such as that presently claimed by Applicants. Like Wang, Cooper also teaches a different type of composition having different component requirements from those of Yamada. Cooper teaches compositions for percutaneous delivery of corticosteroids. Cooper's compositions comprise a binary mixture of a diol compound and a cell-envelope disordering compound, as described in Cooper at Cols. 8, lines 50-68 to Col. 9, lines 1-4. Cooper discloses the discovery that a "select number of combinations of a binary penetration system comprising a cell envelope disordering compound and a diol compound, ..., can consistently and dramatically improve the topical delivery of certain corticosteroids. (Col. 3, lines 1-8 of Cooper).

While Applicants' presently claimed composition comprises 15-80% of a waxy substance, Cooper teaches that such waxy substances, (which Cooper calls "excipients"), are capable of significantly interfering with the penetration enhancing abilities of the invention contemplated by Cooper. (*See*, Cooper at Col. 10, lines 40-42). Cooper further teaches that while a certain level of excipients such as waxy substances may be tolerated in a system, such ingredients "should generally be avoided, "used as sparingly as possible", or limited to less than about 5 or 10%. (*See*, Col. 10, lines 30-34 and lines 49-54 of Cooper). As Cooper explains, this is because such waxy compounds inhibit the ability of the cell-envelope disordering compound to effectively disrupt the intercellular lipid structure of the stratum corneum by preventing the cell-envelope disordering compound from reaching the lipids of the

stratum corneum, perhaps by selective competitive. (*See*, Col. 10, lines 15-49 of Cooper). Thus, it would be readily apparent to one having skill in the relevant art that the use of a high percentage of waxy substance, such as in Applicants' presently claimed composition, is antithetical to the formulation and function of Cooper's described compositions.

It is submitted that there is no teaching, suggestion, or incentive provided by the combination of Yamada, Wang and Cooper to combine the disparate teachings of these cited references to allow one skilled in the art to arrive at Applicants' claimed invention with the required reasonable expectation of success. The combined teachings of these cited references, when considered in their entirety, would not produce, or motivate one having skill in the pertinent art to produce Applicants' claimed composition and its elements, considered as a whole.

Indeed, absent some teaching, suggestion, or incentive supporting the combination, obviousness cannot be established by combining the teachings of the prior art. *In re Geiger*, 815 F.2d 686, 688 2 USPQ2d 1276, 1278 (Fed. Cir. 1987).

Based on the above discussion, it is clear that a combination of Yamada in view of Wang and Cooper, considered in their entirety, does not make obvious Applicants' presently claimed invention considered as a whole. Combining Yamada with Wang, which teaches a lipophilic stick containing a significantly different amount of ingredients compared with Applicants' claimed composition, does nothing to compensate for the deficiencies of Yamada as the primary reference. Furthermore, if one skilled in the art were to use the amount of alkylene glycol as taught by Wang, Applicants' presently claimed compositions would not be achieved, because Applicants have demonstrated that a composition comprising less than about 12% alkylene glycol results in low pharmaceutical activity. (*See*, the instant specification, Example 1, pages 12-13).

Cooper, which teaches that the inclusion of a waxy substance selectively competes with the cell-envelope disordering ingredient, does not make up for the deficiencies of Yamada and Wang, which together would require that a super water-absorbent resin be used in a composition with a pharmaceutically acceptable ingredient, a water soluble absorption enhancer, a fat soluble absorption enhancer and a lower alcohol, with amounts of ingredients

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unlike those of the presently claimed invention. Not only does the combination of Yamada, Wang and Cooper not teach Applicants' presently claimed invention, these references in combination do not suggest Applicants' composition, considered as a whole, absent the very teaching that is found in Applicants' own disclosure. A consideration of the disclosures of Yamada, Wang and Cooper, in their entireties, reveals that the combination of these references is insufficient for one having skill in the art to make the claimed substitutions and other modifications that are necessary to arrive at Applicants' claimed invention.

Yamada, Wang and Cooper, alone and in combination, teach and suggest compositions that are distinct from Applicants' presently claimed invention. These references, considered alone and in combination, do not provide any motivation for one having skill in the art to make the modifications necessary, i.e., changing and modifying ingredients and specified amounts thereof, that would lead one to realize Applicants' invention as presently claimed.

Accordingly, in view of the foregoing, it is respectfully submitted that the presently claimed invention is not obvious over the cited combination of the Yamada, Wang and Cooper references. Withdrawal of the rejection under 35 U.S.C. §103(a) is thus respectfully requested.

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CONCLUSION

Applicants respectfully submit that this application is now in condition for allowance. An action progressing this application to issue is courteously urged.

Should any additional fees be deemed to be properly assessable in this application for the timely consideration of this Amendment and response, or during the pendency of this application, the Commissioner is hereby authorized to charge any such additional fee(s), or to credit any overpayment, to Deposit Account No. **50-0311**, Reference No. **28069-541 NATL**, Customer No. **34537**.

Should any further extension of time be required for the timely consideration of this Amendment and response, the Commissioner is hereby authorized to grant any such further extension of time, and to charge any additional fee(s) owed by Applicants for such extension of time, to the above-mentioned Deposit Account, Reference and Customer Numbers.

If the Examiner believes that further discussion of the application would be helpful, the Examiner is respectfully requested to telephone the undersigned at (212) 692-6742 and is assured of full cooperation in an effort to advance the prosecution of the instant application and claims to allowance.

Respectfully submitted,

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